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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,655	EVANS, GLEN A.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11.07.2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *3,6,12,15,24,36 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 5, 7- 11, 13, 14, 16- 23, 25-35 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06.13.2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-39, with Thy-1 as the species of immunoglobulin-like domain and species EPO as the species of parent binding polypeptide in the reply of 11.07.2005 is acknowledged.

2. Claims 3, 6, 12, 15, 24, 36 and 40 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction (election) requirement in the reply on April 11th 2005.

3. Claims 1, 2, 4, 5, 7- 11, 13, 14, 16- 23, 25-35 and 37-39 are under examination.

Specification

4. The disclosure is objected to because of the following informalities:

Line 1 on page 10 recites "table 1 sets forth ....". However, the specification does not contain table 1. For the purposes of this office action the "Table 2" indicated n page 10 is considered to be the Table 1 that sets for the exemplary immunoglobulin-like domain ThyOx polypeptides as well their alternatives nomenclature used in the art.

The disclosure is objected to because it contains an embedded hyperlink (page 29 in particular) and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Objections

5. Claims 17, 28 and 38 are objected to because of the following informalities: The instant claims consist of non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 5, 7- 11, 13, 14, 16- 23, 25-35 and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite for reciting "scaffold having two or more solvent exposed loops containing a different CDR from a parent antibody inserted into each of said two or more loops and exhibiting selective binding activity toward a ligand bound by said parent antibody" because the exact meaning of the phrase is not clear. Does this mean that the CDR portions within the scaffold is replaced with the CDRs of the parent antibody such that the resulting antibody binds to the parent antigen? As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the purposes of this office action, the claim is interpreted as "a chimeric antibody consisting of a Thy-1

scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is EPO".

Claim 23 is vague and indefinite for reciting "chimeric Thy-1 binding polypeptide comprising one or more altered immunoglobulin-like domain loop regions of a Thy-1 polypeptide and having selective binding activity toward a non-Thy-1 ligand" because the exact meaning of the phrase is not clear. Does this mean that the CDR portions within the scaffold region of Thy-1 are replaced with the CDRs of the parent antibody such that the resulting antibody binds to the parent antigen? As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the purposes of this office action, the claim is interpreted as "a chimeric antibody consisting of a Thy-1 scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is a non-Thy-1 ligand".

Claims 2, 4 and 38 are vague and indefinite for reciting "functional fragment thereof", because the exact meaning of the phrase is not clear. What function are the claims referring to? Is it the function of ThyOx or the antigen binding CDRs that is being claimed? As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the purposes of this office action, it is interpreted as the functional fragment of ThyOx, Thy-1 in particular.

Claims 5, 14 and 26 are drawn to "a chimeric non-immunoglobulin binding polypeptide, wherein the said two or more solvent exposed loops comprise amino acid residues 47-51, 67-98, 67-98 (Δ81-96) or 130-140". It is not clear as to what the applicant means by 67-98 (Δ81-96) or 130-140. Does the applicant mean that one of the exposed loop consists of "67-80 and amino acid residues 97 and 98" or "residues 130-140"? As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 2, 4, 5, 11, 13, 14, 25, 26 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chimeric non-immunoglobulin binding polypeptide, wherein said immunoglobulin-like domain containing scaffold comprises a Thy-1 polypeptide, does not reasonably provide enablement for a chimeric non-immunoglobulin binding polypeptide, wherein said immunoglobulin-like domain containing scaffold comprises a functional fragment of Thy-1 polypeptide. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The instant claims are drawn to a chimeric non-immunoglobulin binding polypeptide, wherein said immunoglobulin-like domain containing scaffold comprises a Thy-1 polypeptide, or a functional fragment thereof. Thus, the claims are broadly drawn to any scaffold that comprises any fragment of any Thy-1 poplypeptide. As described above, the "functional fragment" of a Thy-1 polypeptide is representative of unknown fragments containing any number of truncated, deleted or substituted amino acid residues.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin. Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411 (1987). Removal of the amino terminal histidine of glucagon substantially decreases

the ability of the molecule to bind to its receptor and activate adenylate cyclase. Lin et al Biochemistry USA Vol 14:1559-1563 (1975).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. Elucidation off the genetic code induces one to believe that one can readily obtain a functional synthetic protein for any known nucleic acid sequence with predictable results. The results of the construction of synthetic proteins remain very unpredictable as Burgess et al, Lazar et al, Schwartz et al and Lin et al conclusively demonstrate.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1, 2, 4, 5, 7-11, 13, 14, 16-23, 25-35 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Koide et al (a) (PGPUB 20020019517; Publication date February 14th, 2002) in view of Koide et al (b) (WO 98/56915; International Publication Date 17 December 1998) and in view of Seki et al (PNAS 1985, 82:6657-6661) and in view of Janda et al (U.S Patent 6,472,147; Filed May 25th, 1999) in view of Fibi et al (U.S. Patent 5,712,370; Date Issued 01/27/1998).

The instant claims are interpreted as drawn to a chimeric antibody consisting of a Thy-1 scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is EPO, wherein the residues of said CDRs comprise amino acid residues 47-51, 67-98, 67-98 or 130-140 within the Thy-1 scaffold. The claims further recite a chimeric antibody consisting of a Thy-1 scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is a non-Thy-1 ligand.

Koide et al (a) teach ~~teach~~h (abstract and paragraphs 22-60 and 98-103, in particular) a fibronectin type III (Fn3) polypeptide monobody and the methods of preparing a Fn3 polypeptide monobody. Further provided is a method of identifying the amino acid sequence of a polypeptide molecule capable of binding to a specific binding partner (SBP) so as to form a polypeptide:SSP complex, and a method of identifying the amino acid sequence of a polypeptide molecule capable of catalyzing a chemical reaction. Koide et al (a) teach the production and selection of binding and catalytic polypeptides by the methods of molecular biology, using both combinatorial chemistry and recombinant DNA for generating polypeptide libraries derived therefrom encoding the molecular scaffolding of Fibronectin Type In (Fn3) modified in one or more of its loop regions. The invention also relates to the "artificial mini-antibodies" or "monobodies," i.e., the polypeptides comprising an Fn3 scaffold onto which loop regions capable of binding to a variety of different molecular structures (such as antibody binding sites) have been grafted. Koide et al (a) further teaches a fibronectin type m (Fn3) polypeptide monobody comprising a plurality of Fn3 .beta.-strand domain sequences that are linked to a plurality of loop region sequences, wherein one or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3. Koide et al (a) teach that the .beta.-strand domains of the monobody have at least about 50% total amino acid sequence homology to the corresponding amino acid sequence of wild-type Fn3's .beta.-strand domain sequences, and that preferably, one or more of the loop regions of the monobody comprise amino

acid residues: i) from 15 to 16 inclusive in an AB loop; ii) from 22 to 30 inclusive in a BC loop; iii) from 39 to 45 inclusive in a CD loop; iv) from 51 to 55 inclusive in a DE loop; v) from 60 to 66 inclusive in an EF loop; and vi) from 76 to 87 inclusive in an FG loop. Koide et al (a) also teach a clone, dubbed Ubi4, dominated the enriched pool of Fn3 variants in which further investigation was focused on this Ubi4 clone wherein Ubi4 contains four mutations in the BC loop (Arg 30 in the BC loop was conserved) and five mutations and three deletions in the FG loop. Thus, Koide et al (a) teach that only 13% (12 out of 94) of the residues were altered in Ubi4 from the wild-type sequence.

Koide et al (a) does not teach that said immunoglobulin-like domain containing scaffold comprises a Thy-1 polypeptide, wherein said two or more solvent exposed loops comprise amino acid residues 47-51, 67-98, 67-98 or 130-140 within the Thy-1 scaffold, wherein said two or more altered solvent exposed loops further comprise a ligand binding domain from a parent binding polypeptide, wherein said parent binding polypeptide is EPO and further the limitations as set forth in claims 2, 4, 5, 11, 13, 14, 16-21, 23, 25-35 and 37-39. These deficiencies are made up for by Koide et al (b), Seki et al, Janda et al and Fibi et al.

Koide et al (b) (pages 15-20 in particular) teach the mutation of Fn3 loops and grafting of Ab loops onto Fn3, wherein the Vh-CDR3 of an anti-hen egg lysozyme antibody D1.3 was chosen to graft onto the Fn3 scaffold without significant loss of stability. Koide et al (b) also teach that Fn3 scaffold is an excellent framework for building specific binding proteins for the reason that it itself is the paradigm of a large subfamily (Fn3 family or s-type Ig family) of the immunoglobulin superfamily (IgSF)

including cell adhesion molecules, cell surface hormone and cytokine receptors, chaperonins and carbohydrate-binding domains.

Seki et al teach (please see introduction in particular) the structure of human Thy-1 gene and teach that Thy-1 is a glycoprotein with a sequence homology to the immunoglobulins and is therefore part of the immunoglobulin supergene family, which includes histocompatability antigens and the T-cell and polymeric Ig receptors. Seki et al teach that because of this homology, it has been proposed that Thy-1, like these other membrane proteins plays a role in cellular interactions and that it may function as an adhesion molecule stabilizing the formation of synapses.

Janda et al teach a technology wherein a collection of different genes including Thy-1 were utilized for construction of fusion immunoglobulins wherein the native immunoglobulin structure, in a heterodimeric V.sub.H -V.sub.L Fv, format can be modified in different ways and screened for specificity and activity. For example, Janda teaches that (paragraphs 21 and 22, in particular) by combinatorial alteration of framework regions (FRs) or other manipulations to reorganize and miniaturize the antibody structure by processes coined "complementarity determining region (CDR) shuffling" and "twinibody" formation, antibody-like secondary structures will emerge that contain new paratopes or entirely different structural elements.

Fibi et al teach Erythropoietin (EPO) peptides and antibodies directed against these peptides (abstract, in particular) and the CDRs of such antibodies.

It would have been prima facie obvious to one of ordinary skill in the art to generate a chimeric antibody consisting of a Thy-1 scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is EPO as taught by Koide et al, Barbas et al, Chaovapong et al and Janda et al.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success to have produced a chimeric antibody comprising an immunoglobulin-like domain containing scaffold wherein two or more CDRs of the scaffold are replaced with the CDRs of a parent antibody of interest from the teachings of Koide et al (a) and Koide et al (b) because Koide et al (a) teach the production and selection of binding and catalytic polypeptides by the methods of molecular biology, using both combinatorial chemistry and recombinant DNA for generating polypeptide libraries derived therefrom encoding the molecular scaffolding of Fibronectin Type In (Fn3) modified in one or more of its loop region, wherein the invention relates to the "artificial mini-antibodies" or "monobodies," i.e., the polypeptides comprising an Fn3 scaffold onto which loop regions capable of binding to a variety of different molecular structures (such as antibody binding sites) have been grafted. Koide et al further teaches a fibronectin type m (Fn3) polypeptide monobody comprising a plurality of Fn3 .beta.-strand domain sequences that are linked to a plurality of loop region sequences, wherein one or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3, and because Koide et al (b)

teach the mutation of Fn3 loops and grafting of Ab loops onto Fn3, wherein the Vh-CDR3 of an anti-hen egg lysozyme antibody D1.3 was chosen to graft onto the Fn3 scaffold without significant loss of stability.

In addition, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to have used the method as taught by Koide et al (a) and Koide et al (b) and combine them with the teachings of Seki et al because Koide et al (a) teach teach the production and selection of binding and catalytic polypeptides (such as "artificial mini-antibodies" or "monobodies,") wherein the. beta.-strand domains of the monobody have at least about 50% total amino acid sequence homology to the corresponding amino acid sequence of wild-type Fn3's .beta.-strand domain sequences, and that preferably, one or more of the loop regions of the monobody comprise amino acid residues: i) from 15 to 16 inclusive in an AB loop; ii) from 22 to 30 inclusive in a BC loop; iii) from 39 to 45 inclusive in a CD loop; iv) from 51 to 55 inclusive in a DE loop; v) from 60 to 66 inclusive in an EF loop; and vi) from 76 to 87 inclusive in an FG loop. Koide et al (a) also teach a clone, dubbed Ubi4, dominated the enriched pool of Fn3 variants in which further investigation was focused on this Ubi4 clone wherein Ubi4 contains four mutations in the BC loop (Arg 30 in the BC loop was conserved) and five mutations and three deletions in the FG loop in addition to teaching that only 13% (12 out of 94) of the residues were altered in Ubi4 from the wild-type sequence, and because Koide et al (b) teach that Fn3 scaffold is an excellent framework for building specific binding proteins for the reason that it itself is the paradigm of a large subfamily (Fn3 family or s-type Ig family) of the immunoglobulin

superfamily (IgSF) including cell adhesion molecules, cell surface hormone and cytokine receptors, chaperonins and carbohydrate-binding domains, and because Seki et al teach the structure of human Thy-1 gene and teach that Thy-1 is a glycoprotein with a sequence homology to the immunoglobulins and is therefore part of the immunoglobulin supergene family, which includes histocompatability antigens and the T-cell and polymeric Ig receptors.

Moreover, one of ordinary skill in the art would have known to combine the above teachings of Koide et al (a) with Koide et al (b) and Seki et al because Koide et al (a) and Koide et al (b) collectively teach the production of chimeric antibodies wherein the CDRs can be replaced wherein wherein the Vh-CDR3 of an anti-hen egg lysozyme antibody D1.3 was chosen to graft onto the Fn3 scaffold without significant loss of stability and that this characteristic of Fn3 scaffold being an excellent framework for building specific binding proteins because of being a part of the immunoglobulin superfamily having a Ig-like structure and because Seki et al teach that Thy-1 is a glycoprotein with a sequence homology to the immunoglobulins and is therefore part of the immunoglobulin supergene family, which includes histocompatability antigens and the T-cell and polymeric Ig receptors including that because of this homology, it has been proposed that Thy-1, like these other membrane proteins plays a role in cellular interactions and that it may function as an adhesion molecule stabilizing the formation of synapses.

Furthermore, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to have produced a chimeric

antibody of claim 1, wherein the chimeric antibody consisting of a Thy-1 scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is EPO, wherein the residues of said CDRs comprise amino acid residues 47-51, 67-98, 67-98 or 130-140 within the Thy-1 scaffold because Koide et al (a) teach "artificial mini-antibodies" or "monobodies," comprising an Fn3 scaffold onto which loop regions capable of binding to a variety of different molecular structures (such as antibody binding sites) have been grafted Koide et al (b) teach the mutation of Fn3 loops and grafting of Ab loops onto Fn3, wherein the Vh-CDR3 of an anti-hen egg lysozyme antibody D1.3 was chosen to graft onto the Fn3 scaffold without significant loss of stability and that Fn3 scaffold is an excellent framework for building specific binding proteins because Fn3 is a part of the immunoglobulin superfamily (as evidenced by the instant specification in pages 8-9, bridging paragraph) Seki et al teach that Thy-1 is a glycoprotein with a sequence homology to the immunoglobulins and is therefore part of the immunoglobulin supergene family and teach that because of this homology, it has been proposed that Thy-1, like these other membrane proteins plays a role in cellular interactions and that it may function as an adhesion molecule stabilizing the formation of synapses and because Janda et al teach a technology wherein a collection of different genes, including Thy-1, preferably polypeptide-encoding genes (polypeptide genes), were utilized for construction of fusion immunoglobulins wherein the native immunoglobulin structure, in a heterodimeric V.sub.H -V.sub.L Fv, format can be modified in different ways and screened for specificity and activity, and further because

Fibi et al teach Erythropoietin (EPO) peptides and antibodies directed against these peptides and the CDRs of such antibodies.

Thus it would have been obvious to one skilled in the art to generate a chimeric antibody consisting of a Thy-1 scaffold comprising the CDRs of the parent binding polypeptide wherein the parent binding polypeptide is EPO, wherein the residues of said CDRs comprise amino acid residues 47-51, 67-98, 67-98 or 130-140 within the Thy-1 scaffold as taught by Koide et al (b), Seki et al, Janda et al and Fibi et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

12. No claims are allowed

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

14. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
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LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER